In the Claims

Claim 1 (currently amended):

A device comprising:

a microfluidic substrate comprising at least one sample pathway for sample flow; and

said microfluidic substrate further comprising at least one temperature regulated zone that cycles between at least two different and predetermined temperatures, said at least one temperature regulated zone being adapted to bring at least a portion of said sample pathway to said at least two temperatures while a sample is unidirectionally flowing along said at least a portion of said sample pathway and said at least one temperature regulated zone comprising a metal bar in fluid communication with a plurality of water sources containing water at said at least two temperatures, said metal bar being in thermal communication with said at least a portion of said sample pathway and wherein a sample is cycled between said at least two different and predetermined temperatures while in said at least one temperature regulated zone.

Claim 2 (original):

The device of Claim 1, further comprising a force supplying member operably linked to said at least one pathway for sample flow wherein said force supplying member applies a force to said sample such that said sample travels along said at least one pathway.

Claim 3 (original):

The device of Claim 2, further comprising a sample supplier which supplies a sample to said at least one pathway.

Claim 4 (original):

The device of Claim 3, further comprising at least one inlet basin positioned at a first end of said at least one pathway such that said sample supplier supplies said sample to said inlet basin and said sample travels from said inlet basin to said at least one pathway.

Claim 5 (original):

The device of Claim 4, further comprising at least one outlet basin positioned at a second end of said pathway.

Claim 6 (original):

The device of Claim 5, further comprising at least one reagent supplier positioned between said inlet basin and said outlet basin.

Claim 7 (original):

The device of Claim 6, wherein said device comprises a plurality of said pathways.

Claim 8 (original):

The device of Claim 7, wherein said pathways comprise channels arranged in parallel.

Claim 9 (original):

The device of Claim 8, wherein the force generated by said force supplying member is pressure.

Claim 10 (original):

The device of Claim 1, wherein said microfluidic substrate consists essentially of silicon.

Claim 11 (previously presented):

The device of Claim 1, further comprising a detector for measuring a physicochemical property of a biological sample.

Claim 12 (canceled)

Claim 13 (withdrawn):

A method for conducting a biochemical or chemical process comprising:

cycling at least a portion of at least one sample flow pathway between at least two temperatures while a sample comprising the reagents for said biochemical or chemical process is flowing through said at least a portion of said at least one sample flow pathway.

Claim 14 (withdrawn):

The method of Claim 13, wherein said sample flow pathway is located on a microfluidic substrate.

Claim 15 (withdrawn):

The method of Claim 14, wherein said sample flow pathway is in thermal communication with at least one thermal transfer member which cycles between said at least two temperatures while said sample is continuously flowing through said at least a portion of said at least one sample flow pathway.

Claim 16 (withdrawn):

The method of Claim 15, wherein said thermal transfer member cycles through said at least two temperatures a plurality of times while said sample is continuously flowing through said at least a portion of said at least one sample flow pathway.

Claim 17 (withdrawn):

The method of Claim 16, wherein said thermal transfer member cycles through said at least two temperatures from about 2 to about 35 times while said sample is continuously flowing through said at least a portion of said at least one sample flow pathway.

Claim 18 (withdrawn):

The method of Claim 16, wherein at a portion of a plurality of sample flow pathways are simultaneously cycled between said at least two temperatures while a plurality of samples are simultaneously flowing through said sample flow pathways.

Claim 19 (withdrawn):

The method of Claim 18, wherein said biochemical or chemical reaction comprises a nucleic acid amplification procedure.

Claim 20 (withdrawn):

The method of Claim 19, wherein said nucleic acid amplification procedure comprises polymerase chain reaction.

Claim 21 (withdrawn):

The method of Claim 19 further comprising determining the identity of at least one polymorphic nucleotide in the product of said nucleic acid amplification procedure.

Claim 22 (withdrawn):

A process for carrying out biochemical protocols on at least one sample, comprising:

feeding at least one channel with a continuous flow of a solution containing at least one sample;

injecting at least one reagent from a reagent reservoir into said channel, thereby mixing said sample and said reagent; and

transferring heat between at least one thermal support and at least one temperature regulated portion of said at least one channel.

Claim 23 (withdrawn):

The process according to Claim 22, wherein said feeding comprises applying a pressure difference between a feed basin of said at least one channel and an outlet basin of said at least one channel.

Claim 24 (withdrawn):

The process according to Claim 22, further comprising detecting at least one physicochemical parameter of said sample in said at least one channel.

Claim 25 (withdrawn):

The process according to Claim 22, wherein a temperature of said solution is adjusted to a predetermined level when said solution runs through said at least one temperature regulated portion of said at least one channel.

Claim 26 (withdrawn):

The process according to Claim 22, further comprising cycling said at least one thermal support through at least two different temperatures.

Claim 27 (withdrawn):

The process according to Claim 26, wherein said cycling is repeated 1 to 35 times while solution is running through said at least one portion of said at least one channel.

Claim 28 (withdrawn):

The process according to Claim 22, wherein a plurality of samples separated by separators are sequentially introduced into said at least one channel.

Claim 29 (withdrawn):

The process according to Claim 22, wherein said feeding, said injecting, and said transferring are carried out simultaneously on a plurality of channels arranged in parallel.

Claim 30 (withdrawn):

A process for carrying out in continuous flow at least one temperature cycle on a solution containing at least one sample, comprising:

feeding at least one channel with a continuous flow of said solution;

running said solution through at least one temperature regulated zone; and

cycling said at least one temperature regulated zone successively through a temperature cycle of at least two temperatures in a predetermined temporal series, such that the solution undergoes said temperature cycle at least once in running through the at least one temperature regulated zone once.

Claim 31 (withdrawn):

The process according to Claim 30, further comprising detecting at least one physicochemical parameter of said sample in said channel.

Claim 32 (withdrawn):

The process according to Claim 30, wherein said feeding comprises applying a pressure difference between a feed basin of said at least one channel and an outlet basin of said at least one channel.

Claim 33 (withdrawn):

The process according to Claim 30, wherein said feeding is sequentially repeated with a plurality of samples separated by separators.

Claim 34 (withdrawn):

The process according to Claim 30, wherein said feeding, said running and said cycling are carried out simultaneously on a plurality of channels arranged in parallel.

Claim 35 (withdrawn):

A process for amplifying nucleic acids, comprising:

a) mixing at least one sample comprising said nucleic acids with reagents which are suitable for amplifying nucleic acids to form at least one reaction mixture;

b) feeding at least one channel with a continuous flow of said at least one reaction mixture;

c) running said at least one reaction mixture through at least one temperature regulated zone; and

d) cycling said temperature regulated zone through a temperature cycle of at least two temperatures in a predetermined temporal series, wherein the at least two temperatures, a duration of the temperature cycle, and a rate of said running are preselected such that said at least one nucleic acid sample undergoes a denaturation-hybridization-elongation cycle one or more times while flowing through said at least one temperature regulated zone.

Claim 36 (withdrawn):

The process according to Claim 35, wherein said feeding comprises applying a pressure difference between a feed basin of said at least one channel and an outlet basin of said at least one channel.

Claim 37 (withdrawn):

The process according to Claim 35, wherein said channel is formed in a microfluidic substrate.

Claim 38 (withdrawn):

The process according to Claim 35, wherein said microfluidic substrate consists essentially of silicon.

Claim 39 (withdrawn):

The process according to Claim 35, in which said feeding is sequentially repeated with a plurality of nucleic acid samples separated by separators.

Claim 40 (withdrawn):

The process according to Claim 35, in which steps a), b), c) and d) are carried out simultaneously on a plurality of channels arranged in parallel.

Claim 41 (withdrawn):

A process for identifying in continuous flow at least one nucleotide in at least one target nucleic acid, comprising:

a) feeding a channel with a continuous flow of a solution comprising said at least one target nucleic acid;

b) injecting a microsequencing reagent comprising a microsequencing buffer, at least one microsequencing primer, at least one ddNTP and a polymerase into said channel, thereby mixing said nucleic acid solution and said reagent;

c) running the solution through at least one temperature regulated zone in such a way as to produce at least one cycle comprising denaturation of said at least one target nucleic acid, hybridization of said nucleic acid with said at least one microsequencing primer, and incorporation of a ddNTP which is complementary to the nucleotide to be identified at a 3' end of said primer; and

d) identifying the nucleotide which has been incorporated at the 3' end of the microsequencing primer.

Claim 42 (withdrawn):

The process according to Claim 41, wherein said feeding comprises applying a pressure difference between a feed basin of said channel and an outlet basin of said channel.

Claim 43 (withdrawn):

The process according to Claim 41, further comprising amplifying said at least one target nucleic acid prior to performing said method for identifying at least one nucleotide, wherein said at least one target nucleic acid sequence is amplified using a method comprising:

a) mixing at least one sample comprising said nucleic acids with reagents which are suitable for amplifying nucleic acids to form at least one reaction mixture;

b) feeding at least one channel with a continuous flow of said at least one reaction mixture;

c) running said at least one reaction mixture through at least one temperature regulated zone; and

d) cycling said temperature regulated zone through a temperature cycle of at least two temperatures in a predetermined temporal series, wherein the at least two temperatures, a duration of the temperature cycle, and a rate of said running are preselected such that said at least one nucleic acid sample undergoes a denaturation-hybridization-elongation cycle one or more times while flowing through said at least one temperature regulated zone.

Claim 44 (withdrawn):

The process according to Claim 41, wherein the ddNTPs are labelled with fluorophores and wherein the fluorescence of the incorporated ddNTP is detected.

Claim 45 (withdrawn):

The process according to Claim 44, in which said feeding, said injecting and said running are carried out simultaneously on a plurality of channels arranged in parallel.

Claim 46 (withdrawn):

A process for detecting in continuous flow at least one nucleotide in at least one target nucleic acid, comprising:

a) feeding a channel with a continuous flow of a solution containing at least one target nucleic acid;

b) injecting the reagent for amplifying a region of the at least one target nucleic acid which carries at least one nucleotide to be detected into said channel from a first reagent reservoir;

c) running the solution through at least one temperature regulated zone in such a way that the nucleic acid undergoes a denaturation-hybridization-elongation cycle one or more times;

d) injecting the reagent for purifying the amplification product into said channel from a second reagent reservoir;

e) running the solution through at least one temperature regulated zone to carry out a purification reaction;

f) injecting the microsequencing reagent comprising the microsequencing buffer, at least one microsequencing primer, at least one ddNTP and a polymerase into said channel from a third reagent reservoir;

g) running the reaction mixture through at least one temperature regulated zone in such a way as to produce at least one cycle comprising the denaturation of the target nucleic acid, the hybridization of said nucleic acid with the at least one microsequencing primer, and the incorporation of the ddNTP which is complementary to the nucleotide to be detected, at the 3' end of said primer; and

h) detecting at least one ddNTP which is incorporated at the 3' end of the microsequencing primer.

Claim 47 (withdrawn):

The process according to Claim 46, wherein said feeding comprises applying a pressure difference between a feed basin of said channel and an outlet basin of said channel.

Claim 48 (withdrawn):

The process according to Claim 46, wherein in steps c) and e), the temperature regulated zone is brought successively to at least two temperatures in a temporal series which forms at least one cycle.

Claim 49 (withdrawn):

The process according to Claim 46, wherein the ddNTPs are labelled with fluorophores, and wherein in step h) the fluoresence of the incorporated ddNTP is detected.

Claim 50 (withdrawn):

The process according to Claim 46, wherein the reagent for the purification comprises an exonuclease and an alkaline phosphatase.

Claim 51 (withdrawn):

The process according to Claim 46, wherein steps a), b), c), d), e), f), g) and h) are carried out simultaneously on a plurality of channels arranged in parallel.

Claim 52 (previously presented):

The device of Claim 1, wherein said device comprises a microfluidic substrate comprising at least one temperature regulated zone which is capable of cycling between at least two temperatures, and at least one constant temperature zone.

Claim 53 (previously presented):

The device of Claim 1, wherein said device comprises a microfluidic substrate comprising several temperature regulated zones capable of cycling between at least two temperatures.

Claim 54 (previously presented):

The device of Claim 1, wherein said flowing sample goes through a plurality of temperature cycles as it travels through the temperature regulated zone.

Claim 55 (previously presented):

The device of Claim 8, wherein said channels are fed in series with different samples separated from each other by separators.

Claim 56 (previously presented):

The device of claim 8 wherein the portion of the channel which crosses the temperature regulated zone is rectilinear.

Claim 57 (previously presented):

The device of Claim 1, wherein said device comprises one temperature regulated zone.

Claim 58 (previously presented):

The device of Claim 2, wherein the force generated by said force supplying member is pressure.

Claim 59 (previously presented):

The device of Claim 58, further comprising a sample supplier which supplies a sample to said at least one pathway.

Claim 60 (previously presented):

The device of Claim 59, further comprising at least one inlet basin positioned at a first end of said at least one pathway such that said sample supplier supplies said sample to said inlet basin and said sample travels from said inlet basin to said at least one pathway.

Claim 61 (previously presented):

The device of Claim 60, further comprising at least one outlet basin positioned at a second end of said pathway.

Claim 62 (previously presented):

The device of Claim 61, further comprising at least one reagent supplier positioned between said inlet basin and said outlet basin.

Claim 63 (previously presented):

The device of Claim 62, wherein said device comprises a plurality of said pathways.

Claim 64 (previously presented):

The device of Claim 58, wherein said microfluidic substrate consists essentially of silicon.

Claim 65 (previously presented):

The device of Claim 58, further comprising a detector for measuring a physicochemical property of a biological sample.

Claim 66 (canceled)

Claim 67 (previously presented):

The device of Claim 58, wherein said device comprises a microfluidic substrate comprising at least one temperature regulated zone which is capable of cycling between at least two temperatures, and at least one constant temperature zone.

Claim 68 (previously presented):

The device of Claim 58, wherein said device comprises a microfluidic substrate comprising more than one temperature regulated zone capable of cycling between at least two temperatures.

Claim 69 (previously presented):

The device of Claim 58, wherein said flowing sample goes through a plurality of temperature cycles as it travels through the temperature regulated zone.

Claim 70 (previously presented):

The device of Claim 63, wherein said pathways comprise channels arranged in parallel, and wherein said channels are fed in series with different samples separated from each other by separators.

Claim 71 (previously presented):

The device of Claim 70 wherein the portion of the channel which crosses the temperature regulated zone is rectilinear.

Claim 72 (previously presented):

The device of claim 1, wherein said device further comprises at least one thermostatting means that cycles said temperature regulated zone between said at least two different and predetermined temperatures.

Claim 73 (previously presented):

The device of claim 1, wherein said at least one temperature regulated zone cycles between -5°C and 150°C.

Claim 74 (previously presented):

The device of claim 1, wherein said at least one temperature regulated zone cycles between 20°C and 40°C.

Claim 75 (previously presented):

The device of claim 1, wherein said at least one temperature regulated zone cycles between 57°C, 72°C, and 94°C.

Claim 76 (previously presented):

The device of claim 1, wherein said at least one temperature regulated zone cycles between 37°C and 94°C.

Claim 77 (previously presented):

The device of claim 1, wherein said at least one temperature regulated zone cycles between 55°C and 94°C.

Claim 78 (previously presented):

The device of claim 1, wherein said at least one temperature regulated zone cycles between 65°C and 94°C.

Claims 79-86 (canceled)

Claim 87 (previously presented):

The device of claim 1, wherein said at least one of temperature regulated zone cycles at 25°C and 42.5°C.

Claim 88-89 (canceled)

Claim 90 (previously presented):

The device of claim 1, wherein said device further comprises temperature sensors in each temperature regulated zone.

Claim 91 (previously presented):

The device of claim 90, wherein said temperature sensors are two thermocouples and a platinum sensor.